

EXHIBIT 2

Douching and Genital Talc Use: Patterns of Use and Reliability of Self-reported Exposure

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Background: Feminine hygiene products contain chemicals that may be harmful to human health. Observational studies of the long-term health effects of such products largely rely on self-reported, recalled exposure. We sought to capture patterns of use over the life course and evaluate the reliability of self-reported data.

Methods: We collected retrospective data on douching and genital talc use in the US-based Sister Study at two-time points and evaluated the consistency of reporting. At enrollment (2003–2009), participants were asked to report use in the last year and during ages 10–13. On a follow-up questionnaire (2017–2019), participants were asked about their use of douche or genital talc over their lifetimes.

Results: Among 36,202 women who completed both questionnaires, 14% initially reported ever douching and 27% initially reported ever using genital talc. On the follow-up questionnaire, 51% of participants reported ever douching and 32% reported ever using genital talc. Comparisons across the two questionnaires for use in the year before enrollment showed good consistency, with 90% providing the same responses about douching and 87% providing the same responses about genital talc use. Reliability did not vary by cancer status, race and ethnicity, attained education, or age, though there was some evidence of recall bias for genital talc use among ovarian cancer survivors.

Conclusions: Classification of ever use of feminine hygiene products may be recalled with good consistency, but agreement was lower for specific time periods and trends may vary by subgroup. These potential differences warrant careful consideration in future studies.

Keywords: Douching; Feminine hygiene products; Genital talc; Personal care products; Reliability

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Feminine hygiene products, such as sanitary products, vaginal wipes, powders, and douches, may be linked to adverse health effects.^{1–4} These products can contain potentially harmful substances, including chemicals with endocrine-disrupting properties (e.g., phthalates, parabens, and phenols),^{5–7} volatile organic compounds (e.g., 1,4-dichlorobenzene),⁸ and carcinogenic substances (e.g., asbestos).^{9,10} Self-identified Black or African American women are more likely to report using feminine care products, with exposure burden disparities further augmented by differences in patterns of use and the chemical properties of products marketed to different groups.^{5–8,11–14}

Studies of the long-term health effects of feminine hygiene product use are inherently based on observational rather than experimental data. Some previous studies have described patterns of use,^{6,11,12,15,16} but none of these have considered use across the life course, which is often a more relevant metric for understanding the health impacts of feminine hygiene product use on chronic disease outcomes. However, if historic use cannot be accurately recalled, measurement error can bias effect estimates, especially if recall reliability differs by outcome status.

Using data from the Sister Study, we examined patterns of use and reliability of recall for two feminine hygiene products thought to be associated with gynecologic cancers^{4,17–22} and other reproductive health-related outcomes^{2,23}: douche and powder applied to the genital area. More specifically, we describe how women of varying ages, racial and ethnic groups, and education levels use these products over their lifetimes and examine how reliably the use of such products can be recalled over time. The latter objective has broad utility for quantifying bias when studying the potential health effects of feminine hygiene products or related exposures.

METHODS

Study Sample

The Sister Study (2003–2009) is a prospective cohort designed to study the environmental and genetic determinants of breast cancer and other chronic diseases. Eligible women had a sister with a history of breast cancer, but had not yet had breast cancer themselves, were 35–74 years of age, and resided in the United States, inclusive of Puerto Rico.

At enrollment, women completed questionnaires via a computer-assisted telephone interview. Use of personal care

products, including use of douche, talcum powder in the genital area, and numerous hair and cosmetic products, was ascertained on a separate self-administered questionnaire. A trained examiner took participants' body measurements and biologic samples. The Sister Study is overseen by the internal review board of the National Institutes of Health and all participants signed written informed consent.

Participants provide basic health information annually, with more detailed questionnaires distributed approximately every 3 years. The fourth detailed follow-up questionnaire (2017–2019) asked for extensive information about the participants' use of douche and talc-related products. The overall response rate was approximately 85%, with follow-up data complete through October 2020 (data release 10.1).

From the initial 50,884 participants, we excluded four women who withdrew from the study, 979 who did not complete the enrollment personal care product questionnaire, and 77 women who were diagnosed with breast cancer before completing enrollment. Of the remaining women ($n = 49,824$), 80% ($n = 40,097$) completed the fourth detailed follow-up questionnaire, 1,832 had died, and 7,895 were lost to follow-up. Of those who completed the fourth detailed follow-up, 3,895 did not answer any of the douching or genital talc-specific questions, leaving us with a final sample size of 36,202 women (75% of initial participants still living).

Douching and Genital Talc Use

The enrollment survey included questions about use of douche and talcum powder on "a sanitary napkin, underwear, diaphragm, cervical cap or directly to your vaginal area" during two reference periods: ages 10–13 and in the 12 months before enrollment. More specifically, women were asked to choose whether they "did not use," "sometimes" used, or "frequently" used douche or genital talc between the ages of 10–13, and if they "did not use," used "less than once a month," "1–3 times per month," "1–5 times per week" or "more than five times per week" in the 12 months before enrollment. For most of the analyses presented here, we categorized women as having ever or never used each product during the period of interest.

Approximately 1500 women enrolled during a trial or "vanguard" phase of the study (2003–2004) responded to slightly different versions of the douching and genital talc use questions. These participants were given a lead-in question about ever use, followed by questions about use during their teen years and in the 12 months before enrollment. As this is a relatively small proportion of the cohort, we made the assumption that use during the teen years was a reasonable proxy for use during ages 10–13 and folded the data into the categories defined by the main cohort. However, we also examined use patterns and reliability in this group separately.

In the fourth detailed follow-up questionnaire, we obtained information on use of douche and talc products over the life course. Participants were asked whether they ever

douched or used talc in the genital area (same wording as enrollment). If they responded in the affirmative, they were asked how old they were when they first used the product and how old they were when they last used the product, with an option to indicate current use. We then asked women to report their use of douche or genital talc during each decade of life (teens through 70s, as applicable), including frequency of use ("once a year or less," "2–11 times per year," "1–3 times per month," or "once a week or more"). If participants were missing information about decade of use, but supplied minimum and maximum ages of use, we assumed they used the product continuously during the interim (<1% of users). We assumed extreme minimum and maximum ages of use within a decade when only decade-based responses were provided (6% of douchers and 9% of talc users).

We additionally asked participants when or why they used douche ("after your menstrual period," "to feel clean," "to reduce vaginal odor," "before sex," "after sex," "to treat vaginal symptoms," and/or "other") and what type of solution they used ("water," "homemade water and vinegar mixture," "commercial water and vinegar product," "commercial scented product," "commercial medicated product such as those containing iodine or betadine," and/or "other"). They could select more than one option. For genital talc use, we included an option for use "to prevent dampness and chafing" and removed the option for "to treat vaginal symptoms." We did not collect information about type of talc product used.

Statistical Analysis

Our initial aim was to describe the use of douche and genital talc across the life course based on the data collected from both questionnaires. As use of douche and genital talc was most common during participants' 20s, we provide more detailed descriptions about use during that decade. We present summaries overall and stratified by self-reported race and ethnicity (Hispanic/Latina, non-Hispanic Black, or non-Hispanic White) and attained education (\leq high school, some college, \geq Bachelor's degree). We additionally considered age at enrollment (<50 years, 50–60 years, or >60 years), region of residence (Northeast, Midwest, South, and West, as defined by the US Census Bureau²⁴), and household income ($<\$50,000$ /year, $\$50–<\$100,000$ /year, $\geq\$100,000$ /year).

For assessments of reliability in self-reported use of douche and talc products over time, we initially focused on use in the 12 months before enrollment, comparing responses from enrollment for this exact period to responses from the fourth detailed follow-up about use during the corresponding decade. Because enrollment was more proximal to this referent time period, we consider use reported on the enrollment questionnaire to be the "gold standard," but use the term "consistency" rather than "accuracy" to describe the proportion of women who provide the same response about use on their follow-up versus enrollment questionnaires. Similarly, we assumed the enrollment questionnaire was the "gold standard"

when calculating estimates of sensitivity, specificity, and positive predictive value (PPV). Last, we evaluated Cohen's Kappa statistics (κ), which measure agreement between two sources.²⁵ All estimates include 95% confidence intervals (CIs).

Because the enrollment questionnaire did not collect information on use between age 14 and >1 year before enrollment, it was possible for a participant to report never use on the enrollment questionnaire and ever use on the follow-up questionnaire without contradicting themselves. Bearing this in mind, we also wanted to capture how consistently women could report ever versus never use across the life course even if their reported ages of use did not perfectly match. For this comparison, women were only considered inaccurate if they (1) reported never use in the last 12 months on the enrollment questionnaire but reported using in the 12 months before enrollment on the follow-up questionnaire or (2) reported using in the 12 months before enrollment on the enrollment questionnaire but reported never using on the follow-up questionnaire. Because there was minimal overlap for the youngest exposure periods assessed on the enrollment (ages 10–13) versus follow-up (teen years) questionnaires, participants were not considered self-contradictory for this reliability measure if they reported use at ages 10–13 on the enrollment questionnaire, but no use during their teen years (follow-up).

Last, we examined how reliability of self-reported douching and genital talc use varied by certain key characteristics, including subsequent cancer status, age, race and ethnicity, attained education, body mass index (BMI), region of residence, and household income. We did so by calculating group-specific estimates of consistency and Kappa statistics (κ). Though the number of women with ovarian cancer was small and the analysis was limited to individuals who survived until the fourth detailed follow-up, we were particularly interested in examining whether recall of genital talc use varied by ovarian cancer status, as this has been proposed as a possible source of bias in previous retrospective case–control studies of the association between talc exposure and ovarian cancer.^{26–28}

RESULTS

On the enrollment questionnaire, 3% of participants reported douching during early adolescence (ages 10–13), with 12% reporting use in the 12 months before enrollment (Table 1). Use was highest among non-Hispanic Black women compared to other racial and ethnic groups (9% ages 10–13 and 33% in the last 12 months). Use also varied by attained education, with 16% of those with a high school degree or less reporting use in the last 12 months, versus 9% of those with at least a bachelor's degree. Women who were younger than 50 at enrollment were more likely to report using douche (4% ages 10–13, 14% in the last 12 months) than women >60 at enrollment (2% ages 10–13, 9% in the last 12 months) (eTable 1; <http://links.lww.com/EDE/C6>). Patterns were similar across categories of household income, with highest use among those

making $<\$50,000$ /year (15% in the last 12 months). Southern participants were also more likely to report using than participants in other regions (15% in the last 12 months vs. 9–11% in the other regions).

According to the fourth detailed follow-up questionnaire, douching was most common during ages 20–29, with 39% reporting ever use during this time. More than half of participants (51%) reported ever using across the life-course, again with the highest frequencies of use seen among non-Hispanic Black women (85% ever use), women with no education beyond high school (60% ever use), women with household incomes $<\$50,000$ (57% ever use), and women living in the South (58% ever use). Among those who reported douching, 80% reported only doing so before menopause.

Participants reported that they douched during their 20s “to feel clean” (51%), “to reduce vaginal odor” (32%), “after sex” (30%), “after menstrual period” (29%), and “to treat vaginal symptoms” (16%). The most used products were “commercial water and vinegar products” (38%), “commercial scented products” (30%), and “homemade water and vinegar” (20%). Non-Hispanic Black women and younger women were more likely to report using “commercial water and vinegar products” and using “after menstrual period.”

Genital talc use was common at younger ages, with 19% of women initially reporting that they had used it during early adolescence (Table 2). Fourteen percent reported using the last 12 months. Non-Hispanic Black women were more likely to report using (37% ages 10–13, 20% in the last 12 months) than non-Hispanic White women (18% ages 10–13, 14% in last 12 months) or Hispanic/Latina women (16% ages 10–13, 13% in last 12 months). There were no clear trends by attained education or age group (eTable 2; <http://links.lww.com/EDE/C6>). Participants from the Northeast and South were more likely to use (16% in the 12 months before baseline) than those from the West (11%) or Midwest (13%), and women from lower-income households were more likely to use than women from households with higher incomes.

As with douching, genital talc use was most common during ages 20–29, with 22% of participants reporting use during this time. Overall, 32% reported ever using talc in the genital area (31% non-Hispanic White, 47% non-Hispanic Black, and 29% Hispanic/Latina). The average age at first use was 21.0 years, and while most women only used before menopause (65%), 32% reported using before and after menopause. The most common reasons for use talc during the participants' 20s were “to prevent dampness and chafing” (62%), “to feel clean” (46%), and “to reduce vaginal odor” (33%). Reasons for use were fairly consistent across subgroups defined by race and ethnicity, attained education, age, region of residence, and household income.

Of the 9727 women who did not complete the fourth detailed follow-up, 24% (n = 2309) had died before the mortality cutoff date of January 2020 (eTable 3; <http://links.lww.com/EDE/C6>), including 112 women who reported an

incident ovarian cancer diagnosis. Compared to the included sample, participants missing follow-up data were also more likely to be older, to have a higher BMI, to have lower attained education, to have a lower household income, and to identify as a race and ethnicity other than non-Hispanic White. Participants who completed the fourth follow-up questionnaire except for the talc and douching-related questions ($n = 3,895$), were more likely to have high BMI, lower household income, and to identify as a race and ethnicity other than non-Hispanic White. They were also more likely to have reported douching or genital talc use at enrollment.

We observed good consistency between self-reported douching in the 12 months before enrollment, as recorded on the two questionnaires, with 90% (95% CI = 90%, 91%; Table 3) of individuals providing the same response on the follow-up questionnaire as they did on the enrollment

questionnaire. Kappa statistics indicated moderate agreement ($\kappa = 0.49$, 95% CI = 0.48, 0.51). Specificity was high (96%; 95% CI = 95%, 96%) indicating that those who initially reported never using could reliably recall that information later. PPV was 60% (95% CI = 59%, 62%), meaning that 60% of the women who reported using in the 12 months before enrollment on the follow-up questionnaire had originally self-reported using during that time on the enrollment questionnaire.

Recall of genital talc use was slightly less consistent, with 87% of women (95% CI = 86%, 87%) providing the same response at follow-up as they did at enrollment. Specificity was 94% (95% CI = 94%, 95%), PPV was 53% (95% CI = 51%, 54%), and κ was 0.38 (95% CI = 0.36, 0.39). Here, the largest source of inconsistency was 3,049 women (10% of the sample) who initially reported using genital talc in the 12

TABLE 1. Self-reported Douching by Race and Ethnicity and Educational Attainment Among Women Participating in the Sister Study (Enrolled 2003–2009)

	Self-reported Race and Ethnicity			Attained Education			
	All (n = 36,202)	Hispanic/ Latina (n = 1,293) (4%)	Non-Hispanic Black (n = 2,271) (6%)	Non-Hispanic White (n = 31,808) (88%)	≤High School (n = 4,899) (14%)	Some College (n = 11,480) (32%)	≥Bachelor's Degree (n = 19,816) (55%)
Douching history reported at enrollment							
Ever use during early adolescence (10–13), N (%)	1,025 (3)	31 (2)	204 (9)	765 (2)	156 (3)	393 (3)	476 (2)
Frequency of use in 12 mo before enrollment							
Never	31,854 (88)	1,057 (82)	1,503 (67)	28,585 (90)	4,086 (84)	9,763 (85)	17,998 (91)
Sometimes (<1 time/mo)	3,316 (9)	164 (13)	549 (24)	2,515 (8)	619 (13)	1,297 (11)	1,400 (7)
Frequently (≥1 time/mo)	867 (2)	61 (5)	200 (9)	577 (2)	175 (4)	366 (3)	326 (2)
Ever use, ^a N (%)	4,967 (14)	242 (19)	875 (39)	3,712 (12)	905 (19)	1,949 (17)	2,113 (11)
Douching history reported on fourth detailed follow-up questionnaire							
Ever use, N (%)	18,281 (51)	609 (47)	1,927 (85)	15,334 (49)	2,932 (60)	6,634 (58)	8,711 (44)
Use in teens, N (%)	5,283 (15)	154 (12)	833 (37)	4,156 (13)	935 (19)	2,063 (18)	2,284 (12)
Use in 20s, N (%)	13,883 (39)	391 (31)	1,638 (73)	11,522 (36)	2,194 (45)	5,149 (45)	6,536 (33)
Use in 30s, N (%)	9,566 (27)	339 (27)	1,258 (56)	7,735 (25)	1,658 (34)	3,636 (32)	4,270 (22)
Use in 40s, N (%)	5,749 (16)	232 (18)	874 (39)	4,508 (14)	1,040 (22)	2,243 (20)	2,466 (13)
Use in 50s, ^b N (%)	3,165 (9)	109 (9)	537 (25)	2,426 (8)	607 (13)	1,248 (11)	1,310 (7)
Use in 60s, ^b N (%)	1,517 (5)	45 (5)	263 (16)	1,162 (5)	283 (7)	610 (7)	624 (4)
Use in 70s, ^b N (%)	565 (4)	17 (5)	90 (14)	438 (3)	116 (5)	228 (5)	221 (3)
Among ever users (as reported at follow-up), n = 18,275							
Age at first use, mean (SD)	22.4 (7.0)	24.5 (8.6)	19.8 (5.1)	22.7 (7.1)	22.2 (7.1)	22.1 (6.8)	22.8 (7.2)
Age at last use, mean (SD)	38.2 (14.8)	40.0 (14.6)	42.6 (15.6)	37.5 (14.6)	40.3 (15.3)	40.0 (15.0)	36.9 (14.4)
Douching history relative to menopause, N (%)							
Premenopausal only	14,406 (80)	456 (76)	1,335 (70)	12,308 (81)	2,154 (75)	5,091 (78)	7,157 (83)
Pre- and Postmenopausal	3,513 (19)	131 (22)	560 (29)	2,728 (18)	699 (24)	1,415 (22)	1,399 (16)
Postmenopausal only	166 (1)	10 (2)	7 (0)	145 (1)	27 (1)	54 (1)	85 (1)

(Continued)

TABLE 1. (Continued)

	Self-reported Race and Ethnicity			Attained Education			≥Bachelor's Degree (n = 19,816) (55%)
	All (n = 36,202)	Hispanic/ Latina (n = 1,293) (4%)	Non-Hispanic Black (n = 2,271) (6%)	Non-Hispanic White (n = 31,808) (88%)	≤High School (n = 4,899) (14%)	Some College (n = 11,480) (32%)	
Frequent user (≥ 1 time/mo) during 20s	3,246 (24)	88 (24)	575 (37)	2,480 (22)	659 (31)	1,295 (26)	1,291 (20)
Reason for douching in 20s ^a							
After menstrual period	4,073 (29)	122 (34)	803 (51)	2,936 (26)	697 (33)	1,608 (32)	1,673 (26)
To feel clean	7,044 (51)	180 (50)	895 (57)	5,680 (51)	1,112 (53)	2,630 (53)	3,179 (50)
To reduce vaginal odor	4,499 (32)	101 (28)	569 (36)	3,648 (33)	655 (31)	1,685 (34)	2,079 (33)
Before sex	692 (5)	16 (4)	83 (5)	561 (5)	109 (5)	297 (6)	275 (4)
After sex	4,130 (30)	98 (27)	592 (38)	3,226 (29)	633 (30)	1,525 (31)	1,857 (29)
To treat vaginal symptoms	2,194 (16)	39 (11)	182 (12)	1,879 (17)	254 (12)	723 (15)	1,175 (18)
Other reasons	309 (2)	10 (3)	16 (1)	259 (2)	34 (2)	92 (2)	169 (3)
Type of douche used in 20s ^c							
Water	2,119 (15)	45 (12)	169 (11)	1,812 (16)	329 (16)	715 (14)	1,029 (16)
Water and vinegar, homemade	2,818 (20)	51 (14)	447 (29)	2,187 (20)	414 (20)	1,039 (21)	1,290 (20)
Water and vinegar, commercial	5,257 (38)	180 (49)	838 (54)	4,024 (36)	772 (37)	1,977 (40)	2,420 (38)
Commercial scented	4,137 (30)	106 (29)	453 (29)	3,425 (31)	622 (30)	1,560 (31)	1,901 (30)
Commercial medicated	1,131 (8)	27 (7)	192 (12)	865 (8)	147 (7)	427 (9)	542 (9)
Other solution	363 (3)	7 (2)	26 (2)	310 (3)	47 (2)	112 (2)	191 (3)

Participants were excluded if they withdrew from the study (n = 4), did not complete the enrollment personal care product questionnaire (n = 979), had pre-enrollment breast cancer or ambiguous breast cancer diagnosis or timing of diagnosis (n = 77), did not complete the fourth follow-up questionnaire (n = 9727) or were missing responses for the talc and douching questions on detailed follow-up 4 (n = 3895).

Missing data: 825 women reported a race and ethnicity other than non-Hispanic White, non-Hispanic Black, or Hispanic/Latina. Five women were missing race and ethnicity data; 7 women missing attained education.

Missing data at enrollment: douching as adolescent = 359, douching last 12 months = 165, ever douching = 155.

Missing data at detailed follow-up 4: ever douching = 220, douching as teen = 287, douching in 20s = 281, douching in 30s = 286, douching in 40s = 292, douching in 50s = 295 (716 ineligible), douching in 60s = 269 (7,611 ineligible), douching in 70s = 180 (22,192 ineligible), age at first douche = 121, age at last douche = 198, frequency of douching in 20s (among users) = 450.

^aEver users reported using in the last 12 months or during adolescence.

^bAmong those who had reached that age group.

^cCould select more than one option; percentages add up to more than 100%.

months before enrollment but later responded that they did not use it during this period.

To better understand whether such discrepancies were due to generally poor recall or if participants simply had difficulty recalling exact ages of use, we re-calculated reliability estimates based on the previously described looser reliability criteria that factored in adolescent use and counted women as accurate reporters if they reported using on both questionnaires, even if ages of reported use did not directly overlap. Here, all measures of reliability improved for measures of douching exposure (Table 4), with 95% consistency (95% CI = 95%, 95%), $\kappa = 0.80$ (95% CI = 0.79, 0.81), and PPV increasing to 77% (95% CI = 76%, 78%). The reliability of genital talc use was also higher for this approach (consistency = 86%, 95% CI = 86%, 87%; $\kappa = 0.62$, 95% CI = 0.61, 0.63; PPV = 82%, 95% CI = 81%, 83%). Here the major source of error was again women who initially reported use of talc in the genital area on the enrollment questionnaire, but later reported that they never used it (n = 3626). Further investigation showed that the majority

of these (n = 2544) were women who initially said they used talc at ages 10–13.

Within the vanguard group, 75% reported ever douching. Thirty-two percent of women who ever used said they did so during their teens and 21% used it in the 12 months before enrollment (eTable 4; <http://links.lww.com/EDE/C6>). More than half (54%) of those who reported ever douching denied doing so during those specified time periods. For genital talc use, 44% of vanguard participants reported ever using, with 75% of users stating they did so during their teens and 41% stating they did so in the 12 months before enrollment. Twelve percent of genital talc users only used it at times other than those specified time periods. Estimates of reliability were lower in the vanguard group than in the overall cohort (eTable 5; <http://links.lww.com/EDE/C6>).

When we examined group-specific consistency and κ (eTable 6; <http://links.lww.com/EDE/C6>), we did not see obvious differences in reliability according to cancer status, age, race and ethnicity, attained education, BMI category, region of residence, or household income. As a possible exception, the

TABLE 2. Self-reported Genital Talc Use by Race and Ethnicity and Educational Attainment Among Women Participating in the Sister Study (Enrolled 2003–2009)

	Self-reported race and ethnicity			Attained education		
	All (n = 36,202)	Non-Hispanic		≤High School (n = 4,899) (14%)	Some College (n = 11,480) (32%)	≥Bachelor's Degree (n = 19,816) (55%)
		Hispanic/ Latina (n = 1,293) (4%)	Black (n = 2,271) (6%)			
History of genital talc use reported at enrollment						
Ever use during early adolescence (10–13), N (%)	6,670 (19)	203 (16)	807 (37)	5,545 (18)	870 (19)	2,207 (20)
Frequency of use in 12 mo before enrollment						
Never	31,001 (86)	1,109 (87)	1,817 (80)	27,351 (86)	4,114 (84)	9,596 (84)
Sometimes (<1 time/mo)	2,234 (6)	65 (5)	161 (7)	1,965 (6)	296 (6)	811 (7)
Frequently (≥1 time/mo)	2,826 (8)	108 (8)	282 (12)	2,377 (8)	466 (10)	1,035 (9)
Ever use, ^a N (%)	9,748 (27)	311 (24)	1,012 (45)	8,247 (26)	1,360 (28)	3,322 (29)
History of genital talc use reported on fourth detailed follow-up questionnaire						
Ever use, N (%)	11,409 (32)	374 (29)	1,065 (47)	9,736 (31)	1,620 (33)	3,989 (35)
Use in teens, N (%)	6,438 (18)	210 (16)	731 (32)	5,370 (17)	830 (17)	2,215 (19)
Use in 20s, N (%)	8,002 (22)	255 (20)	827 (37)	6,757 (21)	1,123 (23)	2,852 (25)
Use in 30s, N (%)	6,416 (18)	219 (17)	593 (26)	5,483 (17)	957 (20)	2,351 (21)
Use in 40s, N (%)	4,771 (13)	158 (12)	362 (16)	4,157 (13)	755 (16)	1,779 (16)
Use in 50s, ^b N (%)	3,541 (10)	116 (9)	238 (11)	3,113 (10)	582 (12)	1,368 (12)
Use in 60s, ^b N (%)	2,224 (8)	68 (8)	138 (8)	1,979 (8)	392 (10)	838 (9)
Use in 70s, ^b N (%)	1,123 (8)	29 (9)	51 (8)	1,026 (8)	212 (9)	426 (10)
Among ever users (as reported at follow-up), n =						
11,409						
Age at first use; Mean (SD)	21.0 (11.2)	21.7 (12.1)	17.9 (7.3)	21.3 (11.5)	21.9 (11.7)	21.1 (11.1)
Age at last use; Mean (SD)	43.9 (18.5)	43.7 (17.3)	38.6 (16.6)	44.1 (18.6)	47.0 (19.2)	45.2 (18.3)
Genital talc use relative to menopause, N (%)						
Premenopausal only	7,164 (65)	234 (64)	784 (75)	6,005 (64)	899 (58)	2,363 (61)
Pre- and postmenopausal	3,513 (32)	113 (31)	245 (24)	3,078 (33)	594 (38)	1,359 (35)
Postmenopausal only	410 (4)	17 (5)	12 (1)	371 (4)	69 (4)	141 (4)
Frequent user (≥1 time/mo) during 20s ^c	4,782 (62)	151 (64)	533 (68)	3,985 (61)	701 (65)	1,709 (63)
Reason for genital talc use during 20s^c						
After menstrual period	951 (12)	28 (11)	152 (18)	742 (11)	161 (14)	383 (13)
To feel clean	3,685 (46)	110 (43)	468 (57)	3,036 (45)	542 (48)	1,332 (47)
To reduce vaginal odor	2,677 (33)	61 (24)	315 (38)	2,244 (33)	398 (35)	958 (34)
Before sex	203 (3)	6 (2)	25 (3)	168 (2)	37 (3)	84 (3)
After sex	320 (4)	10 (4)	42 (5)	258 (4)	48 (4)	131 (5)
To prevent dampness and chafing	4,985 (62)	137 (54)	492 (59)	4,243 (63)	625 (56)	1,774 (62)
Other reasons	327 (4)	8 (3)	42 (5)	271 (4)	38 (3)	122 (4)

Participants were excluded if they withdrew from the study (n = 4), did not complete the enrollment personal care product questionnaire (n = 979), had pre-enrollment breast cancer or ambiguous breast cancer diagnosis or timing of diagnosis (n = 77), did not complete the fourth follow-up questionnaire (n = 9,727) or were missing responses for the talc and douching questions on detailed follow-up 4 (n = 3,895).

Missing data: 825 women reported a race and ethnicity other than non-Hispanic White, non-Hispanic Black, or Hispanic/Latina. Five women were missing race and ethnicity data; 7 women missing attained education.

Missing data at enrollment: genital talc use as adolescent = 1,394, genital talc use last 12 months = 139, ever genital talc use = 136.

Missing data detailed at follow-up 4: ever genital talc use = 182, genital talc use as teen = 247, genital talc use in 20s = 248, genital talc use in 30s = 248, genital talc use in 40s = 252, genital talc use in 50s = 249 (716 ineligible), genital talc use in 60s = 222 (7,611 ineligible), genital talc use in 70s = 124 (22,191 ineligible), age at first genital talc use = 316, age at last genital talc use = 332, frequency of genital talc use in 20s (among users) = 301.

^aEver users reported using in the last 12 months or during adolescence.

^bAmong those who had reached that age group

^cCould select more than one option; percentages add up to more than 100%

TABLE 3. Douche and Genital Talc Use in the 12 Months Before Enrollment, as Reported at Enrollment (2003–2009) Versus on the Fourth Detailed Follow-up Questionnaire (2018–2019), n = 36,202

	Douching Use, as Reported at Enrollment		Genital Talc Use, as Reported at Enrollment	
	Non-user in 12 mos prior (n = 31,854) (88%)	User in 12 mos prior (n = 4,183) (12%)	Non-user in 12 mos prior (n = 31,001) (86%)	User in 12 mos prior (n = 5,062) (14%)
Use, as reported at follow-up ^a				
Non-user in 12 mos before enrollment, N (% of total)	29,776 (85)	2,031 (6)	29,018 (81)	3,049 (10)
User in 12 mos before enrollment, N (% of total)	1,341 (4)	2,044 (6)	1,772 (5)	1,973 (6)
Consistency ^b (95% CI)	0.90 (0.90, 0.91)		0.87 (0.86, 0.87)	
Kappa (95% CI)	0.49 (0.48, 0.51)		0.38 (0.36, 0.39)	
Sensitivity (95% CI)	0.50 (0.49, 0.52)		0.39 (0.38, 0.41)	
Specificity (95% CI)	0.96 (0.95, 0.96)		0.94 (0.94, 0.95)	
Positive predictive value (95% CI)	0.60 (0.59, 0.62)		0.53 (0.51, 0.54)	

Missing: 165 women missing enrollment douching status, 139 missing enrollment genital talc status. Additionally, 845 women are missing data on ages of use for douche, and 251 women are missing data for ages of genital talc use.

^aBased on self-reported use during the decade corresponding the participant's age 1 year before enrollment; filled in missing data based on age at first and last use (assuming continuous use).

^bConsistency defined as the proportion of women providing the same response at follow-up versus at enrollment.

TABLE 4. Ever Use of Douche or Genital Talc Across the Life-course, Comparing Self-reports at Enrollment (2003–2009) Versus the Fourth Detailed Follow-up Questionnaire (2018–2019), n = 36,202

	Douching	Enrollment		
		Never	Ever	Missing
Follow-up				
	Never	17,074 (47)	543 (2)	84
	Ever use, 12 mos before enrollment	1,289 (4)	2,540 ^b (7)	21
	Ever use, other ages ^a	12,532 (35)	1,851 (5)	48
	Missing	185	33	2
	Consistency ^c = 0.95 (95% CI = 0.95, 0.95)			
	Kappa = 0.80 (95% CI = 0.79, 0.81)			
	Sensitivity = 0.89 (95% CI = 0.88, 0.90)			
	Specificity = 0.96 (95% CI = 0.96, 0.96)			
	Positive predictive value = 0.77 (95% CI = 0.76, 0.78)			
	Genital talc use	Enrollment		
		Never	Ever	Missing
Follow-up				
	Never	20,895 (58)	3,626 (10)	90
	Ever use, 12 mos before enrollment	1,333 (4)	3,889 ^b (11)	12
	Ever use, other ages ^a	3,957 (11)	2,185 (6)	33
	Missing	133	48	1
	Consistency ^c = 0.86 (95% CI = 0.86, 0.87)			
	Kappa = 0.62 (95% CI = 0.61, 0.63)			
	Sensitivity = 0.63 (95% CI = 0.62, 0.64)			
	Specificity = 0.95 (95% CI = 0.95, 0.95)			
	Positive predictive value = 0.82 (95% CI = 0.81, 0.83)			

Boxes with shading indicate women who reliably reported ever vs. never use. Those in the darker shaded boxes provided the same responses on the enrollment and follow-up questionnaires that were fully consistent with one another. Those in the more lightly shaded box reported use on both questionnaires, but had inconsistent recall about ages of use (i.e., they reported ever using, but said they did not use during the exact time period overlapping with the 12 months before enrollment). Women missing one or both measures were excluded when calculating reliability measures.

^aReported use at ages other than the 12 months before enrollment.

^bIncludes woman who reported using during adolescence on both questionnaires.

^cConsistency defined as the proportion of women providing the same response at follow-up versus at enrollment.

reliability of self-recalled douching was lower among those diagnosed with uterine cancer during the time between enrollment and end of follow-up ($\kappa = 0.68$), compared to the full sample ($\kappa = 0.80$). The reliability measures for genital talc use were similar for ovarian cancer (consistency = 85%, $\kappa = 0.66$) compared to the full sample (consistency = 86%, $\kappa = 0.62$). However, while self-reported use in the 12 months before enrollment was more commonly reported on the enrollment questionnaire (27%) relative to the fourth detailed follow-up questionnaire (21%) in the full sample, the trend was reversed among those with intervening ovarian cancer diagnoses, with 28% self-reporting genital talc use at enrollment and 33% self-reporting genital talc use on the follow-up questionnaire. This was the only subgroup for which the proportion of users increased between enrollment and follow-up and could indicate recall bias (i.e., over-reporting of talc use among those with a history of ovarian cancer). That being said, these numbers may not represent all ovarian cancer cases, as approximately half of the women diagnosed with ovarian cancer after enrollment expired before receiving the fourth follow-up questionnaire.

DISCUSSION

In this assessment of self-reported douching and genital talc use, we described patterns of use across the life course in a diverse group of US women. We additionally examined how reliably women could recall their exposure to these products. Our aim was to help inform and improve future research on the health effects of these and other personal care products, and to help guide public health interventions designed to reduce the use of potentially harmful products.

Both douching and genital talc were widely used in our cohort, with highest use occurring between ages 20 and 29. Younger women and those with fewer years of school were more likely to douche, but there were no consistent patterns in genital talc use by age or attained education. Use of douche dropped dramatically after menopause, but talc use remained fairly common.

Non-Hispanic Black women were more likely to use both types of products, compared to non-Hispanic White women and Hispanic/Latina women. These race and ethnicity trends are consistent with the results of previous studies.^{6,7,11} Though we did not collect data on specific brands or product constituents, prior work has shown that the products marketed to Black/African American women tend to have higher levels of potentially harmful chemicals,^{5,6,14,29} further augmenting the exposure burden for this demographic group.⁷

Women were fairly consistent in their reported use of both products, and reliability improved further when more general classifications of ever versus never use were compared. Discrepancies in self-reported genital talc use were primarily driven by women who initially reported using during early adolescence, but later reported never using. Although it is unclear why this discrepancy arose, measures of reliability

were not systematically different across subgroups defined by cancer status, race and ethnicity, age, attained education, household income, or geographic region, with the noted possible exception for douching among uterine cancer survivors. The observed increase in self-reported genital talc use at follow-up relative to enrollment among ovarian cancer survivors may indicate recall bias is present and potentially driving some of the previously observed differences in effect estimates between studies collecting genital powder exposure status retrospectively versus prospectively.^{26–28}

A major limitation of this analysis was the limited overlap in time periods used to compare use of douching and genital talc, as reported on the enrollment versus follow-up questionnaires. To capture potentially critical windows of early adolescence and recent/adulthood use, the initial questionnaire focused on two narrow time windows: age 10–13 and the 12 months before enrollment. For the follow-up questionnaire, we prioritized getting a full history of use across the life course to augment our existing exposure data. However, with this strategy, we had limited opportunities to measure reliability, especially since 12 months before enrollment age made for a vague benchmark. As such, the second set of reliability estimates, which rely on less stringent criteria for ages of reported use, are likely better metrics for quantifying exposure misclassification.

Our results may not be generalizable, as the Sister Study is a volunteer cohort of women with a first-degree family history of breast cancer that is more highly educated and more likely to be non-Hispanic White than the overall United States.^{30,31} Further, participants who completed the talc and douching-related questions on the fourth detailed follow-up questionnaire were more likely to identify as non-Hispanic White, have a higher attained education, and have a higher household income than the overall Sister Study sample. Although the reliability measures did not vary by these factors, they are all predictors of lower douching and genital talc use at enrollment and therefore may result in selection bias.

We used self-reported race and ethnicity to assign women into broad categories that do not capture the nuances of individuals' lived experiences, especially with regard to their experience with systemic discrimination and perceived cultural norms, both of which influence women's decisions to use certain feminine hygiene products.^{11,32} Furthermore, we were not able to consider differences by sexual orientation or gender identity.

Our greatest strength is our life-course-based approach to examining douching and genital talc use. Some other large cohorts have assessed the duration of genital talc use,^{4,33} but these did not capture more nuanced information on ages or periods of exposure or reasons for use. Douching practices have been assessed in some nationally representative surveys,^{6,16} but most of the existing literature has focused on reproductive-aged women. We know of no other studies of the

reliability of self-reported douching, genital talc use, or any other feminine hygiene products.

Douching and genital talc use were both fairly common in this large, diverse, US-based cohort, with differential patterns of use across groups defined by age, self-reported race and ethnicity, and attained education. We found that women could recall whether they ever used certain feminine hygiene products with good consistency, though agreement was a bit lower when asked to report about specific time periods. The results of this study will help guide future investigations of the health effects of douching, talc, and other feminine hygiene products or personal care products, especially as the field expands to consider patterns across the life course and to quantify the uncertainty of self-reported exposures.

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eTable 1. Self-reported douching by region of residence and household income among women participating in the Sister Study (enrolled 2003-2009)

	All n=36,202	Age at enrollment			Region of residence				Household Income (per year)		
		<50 years n=9,754 (27%)	50-60 years n=14,995 (41%)	>60 years n=11,453 (32%)	Northeast n=6,312 (18%)	Midwest n=10,038 (28%)	South n=11,327 (32%)	West n=8,096 (23%)	<\$50K n=8,026 (22%)	\$50K- <\$100K n=15,098 (42%)	≥\$100K n=13,078 (36%)
Douching history reported at enrollment											
Ever use during early adolescence (10-13); N (%)	1,025 (3)	363 (4)	476 (3)	186 (2)	96 (2)	266 (3)	436 (4)	218 (3)	241 (3)	473 (3)	311 (2)
Frequency of use in 12 months before enrollment											
Never	31,854 (88)	8,350 (86)	13,163 (88)	10,341 (91)	5,747 (91)	8,931 (89)	9,553 (85)	7,294 (90)	6,791 (85)	13,194 (88)	11,869 (91)
Sometimes (<1 time/month)	3,316 (9)	1,115 (11)	1,416 (9)	785 (7)	453 (7)	861 (9)	1,329 (12)	602 (7)	923 (12)	1,454 (10)	939 (7)
Frequently (≥1 time/month)	867 (2)	249 (3)	356 (2)	262 (2)	88 (1)	198 (2)	392 (3)	165 (2)	283 (4)	373 (2)	211 (2)
Ever use ^a ; N (%)	4,967 (14)	1,615 (17)	2,154 (14)	1,198 (11)	616 (10)	1,270 (13)	2,049 (18)	933 (12)	1,363 (17)	2,197 (15)	1,407 (11)
Douching history reported on fourth detailed follow-up questionnaire											
Ever use; N (%)	18,281 (51)	4,462 (46)	8,040 (54)	5,779 (51)	2,705 (43)	4,799 (48)	6,576 (58)	4,007 (50)	4,490 (57)	7,868 (52)	5,923 (45)
Use in teens; N (%)	5,283 (15)	1,781 (18)	2,408 (16)	1,094 (10)	748 (12)	1,321 (13)	2,013 (18)	1,150 (14)	1,320 (17)	2,238 (15)	1,725 (13)
Use in 20s; N (%)	13,883 (39)	3,386 (35)	6,234 (42)	4,263 (38)	2,001 (32)	3,579 (36)	5,167 (46)	3,047 (38)	3,396 (43)	6,000 (40)	4,487 (34)
Use in 30s; N (%)	9,566 (27)	2,029 (21)	4,148 (38)	3,389 (30)	1,330 (21)	2,421 (24)	3,660 (33)	2,039 (25)	2,576 (33)	4,188 (28)	2,802 (22)
Use in 40s; N (%)	5,749 (16)	1,143 (12)	2,416 (16)	2,190 (19)	781 (12)	1,406 (14)	2,306 (21)	1,169 (15)	1,674 (21)	2,504 (17)	1,571 (12)

Water	2,119 (15)	277 (8)	829 (14)	967 (24)	252 (13)	517 (15)	736 (15)	565 (19)	584 (18)	826 (14)	663 (15)
Water and vinegar, homemade	2,818 (20)	382 (11)	1,250 (21)	1,113 (28)	325 (17)	697 (20)	1,004 (20)	715 (24)	797 (25)	1,146 (20)	802 (18)
Water and vinegar, commercial	5,257 (38)	1,909 (57)	2,375 (39)	887 (22)	780 (40)	1,321 (38)	2,059 (41)	970 (33)	1,140 (35)	2,361 (41)	1,670 (38)
Commercial scented	4,137 (30)	1,111 (33)	2,060 (34)	914 (23)	564 (29)	1,089 (31)	1,524 (31)	894 (30)	852 (26)	1,761 (30)	1,472 (34)
Commercial medicated	1,131 (8)	299 (9)	579 (10)	239 (6)	169 (9)	260 (8)	473 (9)	210 (7)	266 (8)	489 (8)	362 (8)
Other solution	363 (3)	52 (2)	140 (2)	158 (4)	66 (3)	91 (3)	100 (2)	91 (3)	93 (3)	149 (3)	108 (2)

Participants were excluded if they withdrew from the study (n=4), did not complete the enrollment personal care product questionnaire (n=979), had pre-enrollment breast cancer or ambiguous breast cancer diagnosis or timing of diagnosis (n=77), did not complete the fourth follow-up questionnaire (n=9,727) or were missing responses for the talc and douching questions on detailed follow-up 4 (n=3,895). Regions of residence are defined by the US census (https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf)

^aEver users reported using in last 12 months or during adolescence

Missing data: 825 women reported a race and ethnicity other than non-Hispanic White, non-Hispanic Black or Hispanic/Latina. 5 women were missing race and ethnicity data; 7 women missing attained education

Missing data at enrollment: douching as adolescent=359, douching last 12 months=165, ever douching=155

Missing data at detailed follow-up 4: ever douching=220, douching as teen=287, douching in 20s=281, douching in 30s=286, douching in 40s=292, douching in 50s=295 (716 ineligible), douching in 60s=269 (7,611 ineligible), douching in 70s=180 (22,192 ineligible), age at first douche=121, age at last douche=198, frequency of douching in 20s (among users)=450

^bAmong those who had reached that age group

^cCould select more than one option; percentages add up to more than 100%

eTable 2. Self-reported genital talc use by region of residence and household income among women participating in the Sister Study (enrolled 2003-2009)

All n=36,202		Age at Enrollment			Region of residence				Household income		
		<50 years n=9,754 (27%)	50-60 years n=14,995 (41%)	>60 years n=11,453 (32%)	Northeast n=6,312 (18%)	Midwest n=10,038 (28%)	South n=11,327 (32%)	West n=8,096 (23%)	<\$50K n=8,026 (22%)	\$50K- <\$100K n=15,098 (42%)	≥\$100K n=13,078 (36%)
History of genital talc use reported at enrollment											
Ever use during early adolescence (10-13); N (%)	6,670 (19)	1,562 (16)	3,029 (21)	2,079 (19)	1,314 (22)	1,699 (18)	2,385 (22)	1,218 (16)	1,484 (19)	2,868 (20)	2,318 (18)
Frequency of use in 12 months before enrollment											
Never	31,001 (86)	8,303 (85)	12,878 (86)	9,820 (86)	5,301 (84)	8,664 (87)	9,473 (84)	7,199 (89)	6,632 (83)	12,855 (85)	11,514 (88)
Sometimes (<1 time/month)	2,234 (6)	683 (7)	938 (6)	613 (5)	424 (7)	621 (6)	741 (7)	427 (5)	557 (7)	968 (6)	709 (5)
Frequently (≥1 time/month)	2,826 (8)	742 (8)	1,121 (8)	960 (8)	563 (9)	714 (7)	1,067 (9)	442 (5)	802 (10)	1,218 (8)	806 (6)
Ever use ^a ; N (%)	9,748 (27)	2,433 (25)	4,202 (28)	3,113 (27)	1,895 (30)	2,575 (26)	3,405 (30)	1,778 (22)	2,337 (29)	4,195 (28)	3,216 (25)
History of genital talc use reported on fourth detailed follow-up questionnaire											
Ever use; N (%)	11,409 (32)	2,975 (31)	5,005 (34)	3,429 (30)	2,120 (34)	3,062 (31)	3,885 (34)	2,234 (28)	2,713 (34)	4,890 (33)	3,806 (29)
Use in teens; N (%)	6,438 (18)	1,892 (19)	2,963 (20)	1,583 (14)	1,301 (21)	1,639 (16)	2,250 (20)	1,202 (15)	1,452 (18)	2,715 (18)	2,271 (17)
Use in 20s; N (%)	8,002 (22)	2,044 (21)	3,620 (24)	2,338 (21)	1,524 (24)	2,094 (21)	2,763 (25)	1,558 (19)	1,880 (24)	3,469 (23)	2,653 (20)
Use in 30s; N (%)	6,416 (18)	1,480 (15)	2,823 (19)	2,113 (19)	1,201 (19)	1,703 (17)	2,211 (20)	1,241 (15)	1,621 (20)	2,777 (19)	2,018 (16)
Use in 40s; N (%)	4,771 (13)	1,084 (11)	1,986 (13)	1,701 (15)	934 (15)	1,266 (13)	1,618 (14)	907 (11)	1,269 (16)	2,099 (14)	1,403 (11)

Use in 50s ^b ; N (%)	3,541 (10)	749 (8)	1,452 (10)	1,340 (12)	699 (11)	923 (9)	1,206 (11)	685 (9)	1,014 (13)	1,527 (10)	1,000 (8)
Use in 60s ^b ; N (%)	2,224 (8)	42 (2)	1,078 (7)	1,104 (10)	431 (9)	586 (8)	738 (8)	445 (7)	707 (10)	950 (8)	567 (6)
Use in 70s ^b ; N (%)	1,123 (8)	--	169 (7)	954 (8)	207 (9)	283 (8)	371 (8)	252 (8)	432 (10)	467 (8)	224 (6)
Among ever users (as reported at follow-up); n=11,409											
Age at first use; Mean (SD)	21.0 (11.2)	19.0 (8.7)	20.2 (9.9)	23.8 (14.0)	20.4 (11.2)	21.5 (11.4)	20.6 (11.0)	21.3 (11.2)	21.9 (11.7)	21.1 (11.1)	20.6 (11.1)
Age at first use; Mean (SD)	43.9 (18.5)	37.3 (14.3)	42.2 (17.1)	52.0 (20.5)	44.5 (18.6)	43.6 (18.3)	43.8 (18.3)	43.6 (18.9)	47.0 (19.2)	45.2 (18.3)	42.1 (18.2)
Genital talc use relative to menopause; N (%)											
Premenopausal only	7,164 (65)	2,218 (77)	3,264 (67)	1,682 (51)	1,294 (63)	1,950 (66)	2,415 (64)	1,440 (66)	1,481 (56)	3,043 (64)	2,640 (71)
Pre and Postmenopausal	3,513 (32)	648 (22)	1,476 (30)	1,389 (42)	705 (34)	898 (30)	1,220 (32)	664 (30)	1,022 (39)	1,539 (32)	952 (26)
Postmenopausal only	410 (4)	32 (1)	146 (3)	232 (7)	66 (3)	119 (4)	137 (4)	80 (4)	125 (5)	179 (4)	106 (3)
Frequent user (≥ 1 time / month) during 20s	4,782 (62)	1,153 (58)	2,147 (62)	1,482 (67)	952 (65)	1,179 (58)	1,691 (64)	921 (61)	1,207 (67)	2,043 (61)	1,532 (60)
Reason for genital talc use during 20s ^c											
After menstrual period	951 (12)	189 (9)	436 (12)	326 (14)	163 (11)	230 (11)	362 (13)	193 (12)	273 (15)	424 (12)	254 (10)
To feel clean	3,685 (46)	970 (47)	1,666 (46)	1,049 (45)	713 (47)	946 (45)	1,341 (49)	655 (42)	886 (47)	1,624 (47)	1,175 (44)
To reduce vaginal odor	2,677 (33)	612 (30)	1,246 (34)	819 (35)	460 (30)	744 (36)	908 (33)	551 (35)	650 (35)	1,169 (34)	858 (32)
Before sex	203 (3)	32 (2)	91 (3)	80 (3)	42 (3)	50 (2)	66 (2)	43 (3)	60 (3)	89 (3)	54 (2)
After sex	320 (4)	45 (2)	136 (4)	139 (6)	57 (4)	73 (3)	105 (4)	84 (5)	94 (5)	144 (4)	82 (3)
To prevent dampness and chafing	4,985 (62)	1,400 (68)	2,273 (63)	1,312 (56)	986 (65)	1,289 (62)	1,680 (61)	999 (64)	1,158 (62)	2,185 (63)	1,642 (62)
Other reasons	327 (4)	78 (4)	144 (4)	105 (4)	64 (4)	76 (4)	117 (4)	68 (4)	85 (5)	123 (4)	119 (4)

Participants were excluded if they withdrew from the study (n=4), did not complete the enrollment personal care product questionnaire (n=979), had pre-enrollment breast cancer or ambiguous breast cancer diagnosis or timing of diagnosis (n=77), did not complete the fourth follow-up questionnaire (n=9,727) or

were missing responses for the talc and douching questions on detailed follow-up 4 (n=3,895). Regions of residence are defined by the US census (https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf)

^aEver users reported using in last 12 months or during adolescence

Missing data: 825 women reported a race and ethnicity other than non-Hispanic White, non-Hispanic Black or Hispanic/Latina. 5 women were missing race and ethnicity data; 7 women missing attained education

Missing data at enrollment: genital talc use as adolescent=1,394, genital talc use last 12 months=139, ever genital talc use=136

Missing data detailed at follow-up 4: ever genital talc use=182, genital talc use as teen=247, genital talc use in 20s=248, genital talc use in 30s=248, genital talc use in 40s=252, genital talc use in 50s=249 (716 ineligible), genital talc use in 60s=222 (7,611 ineligible), genital talc use in 70s=124 (22,191 ineligible), age at first genital talc use=316, age at last genital talc use=332, frequency of genital talc use in 20s (among users)=301

^bAmong those who had reached that age group

^cCould select more than one option; percentages add up to more than 100%

eTable 3. Comparison of participants included in the reliability analysis versus those excluded

	Included (n=36,202)	Did not complete DFU4 (n=9,727)	Did not complete talc/douching questions on DFU4 (n=3,895)
Age at enrollment (years); Mean (SD)	55.6 (8.6)	56.8 (9.9)	53.7 (9.1)
Body mass index (kg/m²), enrollment; Mean (SD)	27.4 (6.0)	28.8 (6.8)	29.0 (6.7)
Follow-up time (years); Mean (SD)	13.0 (1.4)	8.3 (3.8)	13.0 (1.5)
Race and ethnicity; N (%)			
Hispanic/Latina	1,293 (4)	653 (7)	440 (11)
Non-Hispanic Black	2,271 (6)	1,147 (12)	763 (20)
Non-Hispanic White	31,808 (88)	7,577 (78)	2,560 (66)
Attained education, enrollment; N (%)			
≥High school	4,899 (14)	2,114 (22)	656 (17)
Some college or technical school	11,480 (32)	3,907 (40)	1,400 (36)
Bachelor's degree	10,305 (28)	2,116 (22)	1,006 (26)
Graduate degree	9,511 (26)	1,589 (16)	832 (21)
Household income at enrolment (per year); N (%)			
<\$50K	8,026 (22)	3,576 (37)	1,191 (31)
\$50K - <\$100K	15,098 (42)	3,759 (39)	1,523 (39)
≥\$100K	13,078 (36)	2,392 (25)	1,181 (30)
Region of Residence; N (%)			
Northeast (n=6,312)	6312 (18)	1,485 (16)	564 (15)
Midwest (n=10,038)	10,038 (28)	2,504 (26)	943 (25)
South (n=11,327)	11,327 (32)	3,502 (37)	1,501 (41)
West (n=8,096)	8,096 (23)	2,010 (21)	693 (19)
Used douche, ages 10-13; N (%)	1,025 (3)	355 (4)	176 (5)
Used douche, 12 months prior to enrollment; N (%)	4,183 (12)	1,751 (18)	771 (20)
Used genital talc, ages 10-13; N (%)	6,670 (19)	1,761 (19)	829 (22)
Used genital talc, 12 months prior to enrollment; N (%)	5,062 (14)	1,508 (16)	611 (16)
Incident breast cancer; N (%)	2,906 (8)	890 (9)	430 (11)
Incident ovarian cancer; N (%)	125 (0)	136 (2)	15 (0)
Incident uterine cancer; N (%)	278 (1)	90 (1)	34 (1)
Deaths; N (%)	89 (0)	2,309 (24)	11 (0)

Abbreviation: DFU4 = Fourth detailed follow-up

Cut-off for reporting of incident cancers or mortality was September 30, 2019

Missing: Body mass index (9 included, 4 no DFU4, 2 no talc/douching), race and ethnicity (5 included, 4 no DFU4, 3 no talc/douching), education (7 included, 1 no DFU4, 1 no talc/douching), adolescent douching (359 included, 150 no DFU4, 62 no talc/douching), douching in last 12 months (165 included, 74 no DFU4, 30 no talc/douching), genital talc use in adolescence (1,394 included, 410 no DFU4, 136 no talc/douching), genital talc use in last 12 months (139 included, 55 no DFU4, 24 no talc/douching)

eTable 4. Douching and genital talc use in the vanguard group of the Sister Study cohort (n=1,535)

	N (%)
Ever Douched	1,142 (75%)
Ever douched, teen years ^a	357 (32%)
Ever douched, 12 months prior to enrollment ^a	242 (21%)
Used at other times only ^a	597 (55%)
Ever Used Genital Talc	666 (44%)
Ever used genital talc, teen years ^a	485 (75%)
Ever used genital talc, 12 months prior to enrollment ^a	273 (41%)
Used at other times only ^a	75 (12%)

^aAmong ever users

eTable 5. Ever versus never douche and genital talc use in the vanguard group of the Sister Study cohort (n=1,535), as reported at enrollment (2003-2004) versus on the fourth detailed follow-up questionnaire (2018-2019)

	Douching Use, as reported at enrollment		Genital Talc Use, as reported at enrollment	
	Never user n=388 (25%)	Ever User n=1,142 (75%)	Never User n=858 (56%)	Ever User n=666 (44%)
Use, as reported at follow-up				
Never user; N (% of total)	352 (23)	332 (22)	723 (48)	294 (19)
Ever User; N (% of total)	30 (2)	799 (53)	134 (9)	370 (24)
Consistency ^a (95% CI)	0.76 (0.74, 0.78)		0.72 (0.69, 0.74)	
Kappa (95% CI)	0.50 (0.46, 0.54)		0.41 (0.37, 0.46)	
Sensitivity (95% CI)	0.71 (0.68, 0.73)		0.56 (0.52, 0.60)	
Specificity (95% CI)	0.92 (0.89, 0.95)		0.84 (0.82, 0.87)	
Positive Predictive Value (95% CI)	0.96 (0.95, 0.98)		0.73 (0.69, 0.77)	

Missing: 21 women missing enrollment douching status, 14 missing enrollment genital talc status.

^aConsistency defined as the proportion of women providing the same response at follow-up versus at enrollment

eTable 6. Agreement of self-report ever use of douche or genital talc on enrollment questionnaire (2003-2009) versus the fourth detailed follow-up questionnaire (2018-2019), n=36,202

	Douching			Genital Talc Use		
	% used in 12 months prior to enrollment (enrollment / follow-up)	Consistency ^a (95% CI)	κ (95% CI)	% used in 12 months prior to enrollment (enrollment / follow-up)	Consistency ^a (95% CI)	κ (95% CI)
Overall	14% / 16%	0.95 (0.95, 0.95)	0.80 (0.79, 0.81)	27% / 21%	0.86 (0.86, 0.87)	0.62 (0.61, 0.63)
Cancer status						
No ovarian, uterine or breast cancer (n=32,944) ^b	14% / 16%	0.95 (0.95, 0.95)	0.80 (0.79, 0.81)	27% / 21%	0.86 (0.86, 0.87)	0.62 (0.61, 0.63)
Ovarian cancer (n=125) ^b	15% / 19%	0.95 (0.91, 0.99)	0.83 (0.70, 0.96)	28% / 33%	0.85 (0.78, 0.91)	0.66 (0.52, 0.80)
Uterine cancer (n=278) ^b	12% / 15%	0.93 (0.89, 0.95)	0.68 (0.55, 0.81)	32% / 27%	0.86 (0.82, 0.90)	0.67 (0.57, 0.76)
Breast cancer (n=2,906) ^b	14% / 15%	0.95 (0.94, 0.96)	0.80 (0.76, 0.83)	26% / 20%	0.86 (0.85, 0.87)	0.61 (0.58, 0.65)
Age at enrollment						
<50 (n=9,754)	17% / 20%	0.93 (0.93, 0.94)	0.78 (0.76, 0.80)	25% / 20%	0.87 (0.87, 0.88)	0.64 (0.62, 0.66)
50-60 (n=14,995)	14% / 16%	0.95 (0.94, 0.95)	0.80 (0.78, 0.81)	28% / 22%	0.87 (0.86, 0.87)	0.64 (0.63, 0.66)
60+ (n=11,453)	10% / 12%	0.96 (0.96, 0.97)	0.81 (0.80, 0.83)	27% / 19%	0.85 (0.84, 0.85)	0.58 (0.56, 0.60)
Self-reported race and ethnicity						
Non-Hispanic White (n=31,808)	12% / 14%	0.95 (0.95, 0.96)	0.79 (0.78, 0.80)	26% / 20%	0.86 (0.86, 0.87)	0.62 (0.61, 0.63)
Non-Hispanic Black (n=2,271)	39% / 44%	0.91 (0.90, 0.92)	0.81 (0.79, 0.84)	45% / 33%	0.82 (0.80, 0.84)	0.63 (0.59, 0.66)
Hispanic/Latina (n=1,293)	19% / 19%	0.90 (0.89, 0.92)	0.69 (0.64, 0.74)	24% / 19%	0.85 (0.84, 0.87)	0.57 (0.52, 0.63)
Attained education						
≤High school (n=4,899)	18% / 21%	0.93 (0.93, 0.94)	0.79 (0.77, 0.81)	28% / 22%	0.85 (0.84, 0.86)	0.60 (0.57, 0.62)
Some college (n=11,480)	17% / 20%	0.95 (0.94, 0.95)	0.82 (0.81, 0.84)	29% / 23%	0.85 (0.84, 0.86)	0.62 (0.60, 0.63)
≥Bachelor's Degree (n=19,816)	11% / 13%	0.95 (0.95, 0.96)	0.78 (0.76, 0.79)	26% / 19%	0.87 (0.87, 0.88)	0.63 (0.62, 0.64)
Body mass index (kg/m²)						
≤25 (Normal weight) (n=14,924)	11% / 13%	0.95 (0.95, 0.96)	0.78 (0.77, 0.80)	22% / 16%	0.89 (0.88, 0.89)	0.64 (0.62, 0.65)
>25-≤30 (Overweight) (n=11,390)	14% / 16%	0.95 (0.94, 0.95)	0.79 (0.78, 0.81)	27% / 20%	0.86 (0.85, 0.86)	0.60 (0.59, 0.62)
>30 (Obese) (n=9,879)	17% / 20%	0.94 (0.94, 0.95)	0.81 (0.80, 0.83)	35% / 28%	0.83 (0.82, 0.84)	0.60 (0.59, 0.62)
Region of Residence^c						
Northeast (n=6,312)	10% / 12%	0.96 (0.96, 0.96)	0.79 (0.77, 0.82)	30% / 23%	0.85 (0.84, 0.85)	0.60 (0.58, 0.62)
Midwest (n=10,038)	13% / 14%	0.95 (0.95, 0.96)	0.80 (0.78, 0.81)	26% / 20%	0.87 (0.86, 0.88)	0.63 (0.61, 0.65)
South (n=11,327)	18% / 21%	0.94 (0.94, 0.95)	0.81 (0.80, 0.83)	30% / 23%	0.85 (0.84, 0.86)	0.62 (0.60, 0.63)
West (n=8,096)	12% / 14%	0.95 (0.94, 0.95)	0.77 (0.75, 0.79)	22% / 17%	0.88 (0.88, 0.89)	0.63 (0.61, 0.65)

Household income (per year)							
<\$50K (n=8,026)	17% / 19%	0.94 (0.94, 0.95)	0.80 (0.79, 0.82)	29% / 23%	0.84 (0.84, 0.85)	0.59 (0.57, 0.61)	
\$50K - <\$100K (n=15,098)	15% / 17%	0.95 (0.94, 0.95)	0.79 (0.78, 0.81)	28% / 22%	0.86 (0.86, 0.87)	0.63 (0.61, 0.64)	
≥\$100K (n=13,078)	11% / 12%	0.96 (0.95, 0.96)	0.79 (0.78, 0.81)	25% / 18%	0.87 (0.87, 0.88)	0.63 (0.61, 0.65)	

^aConsistency defined as the proportion of women providing the same response at follow-up versus at enrollment

^b29 women had both breast and uterine cancer, 17 had both breast and ovarian cancer, 3 had both ovarian and uterine and 1 had all 3 cancer types

^cRegions of residence defined by the US census (https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf)